REMARKS

Reconsideration of this application, as amended, is respectfully requested.

The Applicants wish to draw the Examiner's attention to the Applicants' related copending applications and issued patents (see Appendix A) directed to nanoparticles and methods of preparation and use thereof. In particular, the Applicant draws the Examiner's attention to the Applicant's own U.S. Patent No. 6,506,564.

The Applicants note that the Examiner did not return executed copies of the PTO 1449 form for the 6th Supplemental IDS that was hand delivered to the Examiner on September 9, 4642. The Applicants request that the Examiner fully execute the PTO 1449 form for the 6th Supplemental IDS and return a copy of the executed PTO 1449 form to the undersigned representative. A copy of the 6th Supplemental IDS, associated PTO 1449 form, and PTO stamped postcard acknowledging receipt of the IDS, PTO 1449 form and references are attached. The Examiner is requested to contact the undersigned representative if the Examiner would like to have another copy of the references.

The specification was amended to update the priority claim, thus obviating the Examiner's objection to the specification. No new matter has been introduced by this amendment.

Claims 185-188 were pending in this application and were cancelled without prejudice or disclaimer. New claims 433-461 were added to further clarify the Applicants' invention. Support for the new claims can be found in the original claims and in the specification, e.g., pages 77-80. Accordingly, no new matter has been introduced into this application as a result of the present amendment.

Turning to the office action, claims 185-188 was rejected under 35 U.S.C. section 102(e) as being anticipated by Yguerabide (U.S. Patent No. 6,214,560)("Yguerabide"). The Applicants respectfully traverse this rejection.

As a general rule, for prior art to anticipate under section 102, every element of the claimed invention must be identically disclosed in a single reference. <u>Corning Glass Works v. Sumitomo Electric</u>, 9 U.S.P.Q.2d 1962, 1965 (Fed. Cir. 1989). The exclusion of a claimed element, no matter how insubstantial or obvious, from a reference is enough to negate anticipation. Connell v. Sears, Roebuck & Co., 220 U.S.P.Q 193, 1098 (Fed. Cir. 1983).

Applicants respectfully submit that Yguerabide cannot be applied to support an anticipation rejection of the new claims under 35 U.S.C. section 102(e).

Specifically, the Examiner alleged that Yguerabide taught detection and measurement of one or more analytes in a sample using particles of specific composition and size using light scattering. The discussion is found starting in col. 82, line 35, of Yguerabide. Col. 83 provides further discussion regarding particle size and particle binding to a surface. There is no discussion of any nanoparticle-oligonucleotide conjugate prepared by the aging process recited in the claims. See claim 433. Nanoparticle-oligonucleotide conjugates prepared by this aging process exhibit melting (dehybridization) profiles that are extremely narrow compared to the profiles obtained using the same oligonucleotides not attached to nanoparticles, and extraordinary selectivity (detection as little as a single base difference) and sensitivity (detecting as little as 10 femtomoles of nucleic acid without amplification) have been obtained using these conjugates in such assays (see particularly Examples 5, 7 and 19) of the application. Moreover, the claimed conjugates are surprisingly more stable compared to conjugates made without the aging step (see, e.g., Example 3 of the application). New claims 433-461 recite limitations that are neither taught, made obvious, or suggested by the cited reference. Thus, the Applicant respectfully submits that Yguerabide cannot be applied to support a section 102(e) rejection of the new claims.

In conclusion, the Applicants respectfully submit that the claims in this application are in allowable condition and request a Notice to this effect.

Reconsideration of this application is respectfully requested and a favorable determination is earnestly solicited. The Examiner is invited to contact the undersigned representative if the Examiner believes that this would be helpful in expediting the prosecution of this application.

Dated:

McDonnell Boehnen Hulbert & Berghoff, Ltd. 300 South Wacker Drive Chicago, IL 60606

Telephone: 312-913-0001 Facsimile: 312-913-0001 Respectfully submitted,

Emily Miao

Reg. No. 35,285



APPENDIX A

| ATTY | Serial No./ | | |
|------------|--|---|---|
| Case No. | Filing Date | Inventors/Title | Status |
| 00-653-A | U.S. 09/927,777 Filed 8/10/01 | Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton, Garamella, Li, Park/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERETO AND USES THEREFORE | PENDING |
| 00-713-B1 | 09/923,625 Filed 8/7/01 | Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERETO AND USES THEREFOR | PENDING |
| 00-713-С | 09/344,667, filed 6/25/99 | Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERETO AND USES THEREFORE | U.S. Patent No. 6,361,944, issued 3/26/02 |
| 00-713-I | U.S.S.N 09/603,830 Filed 6/26/00 | Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton; NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERETO AND USES THEREFOR | U.S. Patent No. 6,506,564, issued 1/14/03 |
| 00-713-I-1 | 09/961,949 9/20/01 | Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton; | U.S. Patent No. 6,582,921, issued June 24, 2003 |

| ATTY | Serial No./ | | |
|------------|-----------------------|-----------------|-------------------|
| Case No. | Filing Date | Inventors/Title | Status |
| | | NANOPARTICLES | |
| | | HAVING | |
| | | OLIGONUCLEOTI | |
| | | DES ATTACHED | |
| | | THERETO AND | |
| | | USES THEREFOR | |
| 00-713-I-2 | 09/957,318 9/20/01 | See 00-713-I-1 | PENDING |
| 00-713-I-3 | 09/957,313 | See 00-713-I-1 | U.S. Patent No. |
| | 9/20/01 | | 6,645,721, issued |
| | | | 11/11/03 |
| 00-713-I-4 | 09/966,491 | See 00-713-I-1 | U.S. Patent No. |
| | 9/28/01 | | 6,610,491 |
| | | | |
| 00-713-I-5 | 09/966,312 | See 00-713-I-1 | ALLOWED |
| | 9/28/01 | | |
| | | | |
| 00-713-I-6 | 09/967,409 | See 00-713-I-1 | PENDING |
| | 9/28/01 | | |
| 00.512.1.5 | 00/074 500 | G., 00 712 I 1 | ALLOWED |
| 00-713-I-7 | 09/974,500 | See 00-713-I-1 | ALLOWED |
| | 10/10/01 | | |
| 00-713-I-8 | 09/974,007 | See 00-713-I-1 | PENDING |
| 00-713-1-0 | 10/10/01 | 366 00-713-1-1 | 1 LINDING |
| | 10/10/01 | | |
| 00-713-I-9 | 09/973,638 | See 00-713-I-1 | PENDING |
| 00-713-1-2 | 10/10/01 | 500 00 715 1 1 | LENDING |
| | 10,10,01 | | |
| 00-713-I- | 09/973,788 | See 00-713-I-1 | ALLOWED |
| 10 | 10/10/01 | | |
| | | | |
| 00-713-I- | 09/975,062 | See 00-713-I-1 | ALLOWED |
| 11 | 10/11/01 | | |
| | | | |
| 00-713-I- | 09/975,376 | See 00-713-I-1 | PENDING |
| 12 | 10/11/01 | | |
| | | | |
| 00-713-I- | 09/975,384 | See 00-713-I-1 | PENDING |
| 13 | 10/11/01 | | |
| 00-713-I- | 00/075 409 | See 00-713-I-1 | ALLOWED |
| UU-/13-1- | 09/975,498 | 366 00-713-1-1 | ALLOWED |

| ATTY | Serial No./ | | |
|-----------|------------------------|--------------------|-------------------|
| Case No. | Filing Date | Inventors/Title | Status |
| 14 | 10/11/01 | | |
| 00-713-I- | 09/975,059 | See 00-713-I-1 | PENDING |
| 15 | 11/11/01 | | |
| | | | |
| 00-713-I- | 09/976,601 | See 00-713-I-1 | PENDING |
| 16 | 10/12/01 | | |
| | | | |
| 00-713-I- | 09/976,968 | See 00-713-I-1 | PENDING |
| 17 | 10/12/01 | | |
| | | | |
| 00-713-I- | 09/976,971 | See 00-713-I-1 | ALLOWED |
| 18 | 10/12/01 | | |
| | | | |
| 00-713-I- | 09/976,863 | See 00-713-I-1 | PENDING |
| 19 | 10/12/01 | | |
| 00.512.1 | 00/07/ 577 | G - 00 712 I 1 | ALLOWED |
| 00-713-I- | 09/976,57.7 | See 00-713-I-1 | ALLOWED |
| 20 | 10/12/01 | | |
| 00-713-I- | 09/976,618 | See 00-713-I-1 | PENDING |
| 21 | 10/12/01 | 366 00-713-1-1 | FENDING |
| 21 | 10/12/01 | | |
| 00-713-I- | 09/981,344 | See 00-713-I-1 | PENDING |
| 22 | 10/15/01 | | |
| | 10/10/01 | | |
| 00-713-I- | 09/976,900 | See 00-713-I-1 | PENDING |
| 23 | 10/12/01 | | |
| | | | |
| 00-713-I- | 09/976,617 | See 00-713-I-1 | PENDING |
| 24 | 10/12/01 | | |
| | | | |
| 00-713-I- | 09/976,378 | See 00-713-I-1 | PENDING |
| 25 | 10/12/01 | | |
| 00.513 | 10/410 224 | G 00 712 I 1 | DENIDRIC |
| 00-713-i- | 10/410,324 | See 00-713-I-1 | PENDING |
| 26 | 04/10/03 | Mirkin, Letsinger, | U.S. Patent No. |
| 00-713-L | U.S.S.N. 09/693,005 | Mucic, Storhoff, | 6,495,324, issued |
| | Filed 10/20/00 | Elghanian/ | 12/17/02 |
| | 11100 10/20/00 | NANOPARTICLES | 12/11/02 |
| | | HAVING | |
| , | | OLIGONUCLEOTI | |
| | | DES ATTACHED | |
| | 1 | 1223.111.101122 | <u> </u> |

| ATTY | Serial No./ | | |
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| Case No. | Filing Date | Inventors/Title | Status |
| | | THERETO AND USES THEREFORE | |
| 00-713-M | U.S.S.N. 09/693,352 Filed 10/20/00 | Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERETO AND USES THEREFORE | U.S. Patent No. 6,417,340, issued 7/9/02 |
| 00-714-G | U.S. 09/830,620 Filed 8/15/01 | Mirkin, Nguyen/ NANOPARTICLES WITH POLYMER SHELLS | PENDING |
| 00-715-A | U.S. 09/760,500 Filed 1/12/01 | Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton; Garamella, Li/ METHOD OF ATTACHING OLIGONUCLEOTI DES TO NANOPARTICLES AND PRODUCTS PRODUCED THEREBY | ALLOWED |
| 00-1085-A | U.S.S.N. 09/820,279 Filed 3/28/01 | Mirkin,Letsinger, etc./ METHOD AND MATERIALS FOR ASSAYING BIOLOGICAL MATERIALS | ALLOWED |
| 00-1086-A | U.S. 09/903,461 Filed 7/11/01 | Letsinger, Garimella/ METHOD OF DETECTION BY ENHANCEMENT OF SILVER STAINING | U.S. Patent No. 6,602,669, Filed 8/5/03 |
| 01-565-A | USSN 10/125,194 Filed 4/18/02 | Mirkin, Nguygen, Watson, Park/ OLIGONUCLEOTI DE-MODIFIED ROMP POLYMERS | PENDING |

| ATTY | Serial No./ | | |
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| Case No. | Filing Date | Inventors/Title | Status |
| | | AND CO- | |
| | | POLYMERS | |
| 01-599-A | U.S.S.N. | Storhoff/NOVEL | PENDING |
| | 10/291,291 | THIOL-BASED | |
| | Filed 11/08/02 | METHOD FOR | |
| | | ATTACHING | |
| | | OLIGONUCLEOTI | |
| | | DES TO | |
| 01 ((1) | HOON | NANOPARTICLES | DENIDING |
| 01-661-A | U.S.S.N. | Mirkin, Cao, Jin/ | PENDING |
| | 10/034,451 | DNA-MODIFIED | |
| | Filed 12/28/01 | CORE-SHELL | |
| | | AG/AU | |
| 01-661-C | U.S.S.N. | NANOCRYSTALS Mirkin, Cao, Jin/ | PENDING |
| 01-001-C | | DNA-MODIFIED | PENDING |
| | 10/153,483 Filed 5/22/02 | CORE-SHELL | |
| | Filed 3/22/02 | AG/AU | |
| | | NANOCRYSTALS | |
| 01-661-E | U.S.S.N. | Mirkin, Cao, Jin/ | PENDING |
| 01-001-E | 10/397,579 | DNA-MODIFIED | LIDING |
| | 3/26/03 | CORE-SHELL | |
| | 3/20/03 | AG/AU | |
| | | NANOCRYSTALS | |
| 01-1565-A | U.S.S.N. | Park, Taton, | PENDING |
| 01 1000 11 | 10/266,983 | Mirkin/ARRAY- | |
| | Filed 10/08/02 | BASED | |
| | | ELECTRICAL | |
| | | DETECTION OF | |
| • | | DNA USING | |
| | | NANOPARTICLE | |
| | | PROBES | |
| 01-1705-A | U.S.S.N. | Nam, Park, | PENDING |
| | 10/108,211 | Mirkin/BIO- | |
| | Filed 3/27/02 | BARCODES | |
| | | BASED ON | |
| | | OLIGONUCLEOTI | |
| | | DE-MODIFIED | |
| | | NANOPARTICLES | PENDONIC |
| 02-338-B | USSN 10/172,428 | Cao, Jin, Nam, | PENDING |
| | Filed 6/14/02 | Mirkin/MULTICHA | |
| | | NNEL DETECTION | |
| | | USING | |
| | | NANOPARTICLE | <u></u> |

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| Case No. | Filing Date | Inventors/Title | Status |
| | | PROBES WITH | |
| | | RAMAN | |
| | | SPECTROSCOPIC | |
| | | FINGERPRINTS | |
| 02-338-C | 10/431,341 | Cao, Jin, Nam, | PENDING |
| | 5/7/03 | Mirkin/MULTICHA | |
| | | NNEL DETECTION | |
| | | USING | |
| | | NANOPARTICLE | |
| | | PROBES WITH | |
| | | RAMAN | |
| | | SPECTROSCOPIC | |
| | | FINGERPRINTS | |